Processors of agricultural products

ADM

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VIA HAND DELIVERY

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Comments to Interim Final Rule for Health Claims: Plant Sterol/Stanol Esters and Coronary Heart Disease; Docket Nos. 00P-1275 and 00P-1276

Dear Sir or Madam:

The Archer Daniels Midland Company ("ADM") submits these comments in response to the Food and Drug Administration's ("FDA") invitation to comment on the Interim Final Rule for Plant Sterol/Stanol Esters and Coronary Heart Disease ("CHD") (hereinafter referred to as the "Interim Final Rule" or "Interim Health Claim") published in the Federal Register on September 8, 2000. 65 Fed. Reg. 54686 (2000).

From the outset, ADM notes its support of the concepts contained in the Interim Final Rule as written. ADM submits these comments, in part, to offer further support for broadening the eligible types of food products which may contain the CHD claim. Separately, ADM also seeks an amendment to the description of the substance that is the subject of this health claim to include non-esterified forms of plant sterols. This change to the "nature of the substance" definition is supported by the scientific evidence presented by the health claim petitioners and acknowledged by FDA which demonstrates the relationship between non-esterified forms of plant sterols and CHD.

A. ACTIONS REQUESTED

Pursuant to the terms of the Interim Final Rule, ADM respectfully submits the following comments in support of:

1. The expansion of the categories of food listed in Interim Final Rule § 101.83(c)(iii)(A) as eligible to bear the plant sterol/stanol ester CHD health claim to include health bars, health drinks and yogurt-type products; and

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2. The expansion of Interim Final Rule § 101.83(c)(ii) to include non-esterified forms of plant sterols within the definition of the substance eligible to make a CHD health claim.

B. DISCUSSION

1. Safety and Analytical Data Support the Expansion of the Categories of Food Eligible to Bear the CHD Health Claim to Include Health Bars, Health Drinks, and Yogurt-Type Products.

The Interim Final Rule authorizes a coronary heart disease health claim for those food products that contain a specified minimum amount of plant sterol/stanol esters. Specifically, the types of food eligible to bear the plant sterol esters/CHD health claim are spreads and dressings for salads; the types of food eligible for the plant stanol esters/CHD health claim are spreads, dressings for salad, snack bars, and dietary supplements in softgel form. See Interim Rule § 101.83(c)(2)(iii)(A)(1) and (2).

In the preamble to the Interim Final Rule, FDA stated that "[i]f comments . . . submit supporting data establishing that the use of plant sterol esters in other food products is safe and lawful and provide a validated analytical method that permits accurate determination of the amount of plant sterol esters in these foods, FDA will consider broadening the categories of foods eligible to bear the claim in the final rule." 65 Fed. Reg. at 54707-08; see also 21 C.F.R. § 101.14(b)(3)(ii). Pursuant to this Federal Register provision, ADM submits the following data and information in support of the expansion of the food categories eligible to bear a plant sterol ester/CHD health claim to include health bars, health drinks and yogurt-type products.

For conventional foods, the evaluation of whether a substance is "safe and lawful" involves a consideration of whether the ingredient that is the source of the substance is generally recognized as safe ("GRAS"), listed as a food additive, or authorized by a prior sanction issued by FDA. Because the list of "safe and lawful" food products incorporating plant sterol esters may increase by virtue of future GRAS notifications, ADM further requests that FDA modify the Interim Health

Claim to authorize the use of the interim CHD health claim on other food products subject to GRAS notifications that have received no objection letters from FDA and have validated analytical methods for determining the amount of plant sterol esters in the food.

a. Safety

Although the original petitioner for the plant sterol esters/CHD health claim, Lipton, only requested authorization to use the health claim in the labeling of spreads and dressings for salad, significant evidence of the safety of plant sterol esters justify the expansion of the Interim Health Claim to include other foods. As discussed in the Federal Register preamble, Lipton submitted a GRAS notification (subsequently converted into a Food Master File) on January 11, 1999, informing FDA of its conclusion that plant sterol esters are GRAS for use as a nutrient in vegetable oil spreads. The Lipton submission was based on a thorough evaluation of the available literature, several unpublished studies which have been subsequently published (Baker, 1999; Hepburn, 1999; Waallkens-Berendsen, 1999; Weststrate, 1999; Ayesh, 1999; Hendricks, 1999; Sanders, 2000) and information from an independent panel of experts retained by Lipton to evaluate the safety data.

On April 30, 1999, FDA responded stating that the agency "has no questions at this time regarding Lipton's conclusion . . . Furthermore, FDA is not aware of any scientific evidence that vegetable oil sterol esters would be harmful." See 65 Fed. Reg. at 54688-89. In a letter dated September 24, 1999, Lipton provided additional information to FDA in support of its conclusion that plant sterol esters are also GRAS for use in dressings for salad.

In the preamble to the Interim Final Rule, FDA acknowledges that a review of Lipton's submissions to the agency "reveal[s] significant evidence supporting the safety of the use of plant sterol esters at the levels necessary to justify a health claim." 65 Fed. Reg. at 54689. Subsequently, two other GRAS notifications on plant sterol esters have been submitted to FDA, one by Cargill, Inc. for the use of

vegetable oil phytosterol esters as a nutrient in vegetable oil spread, salad dressings, bars, and yogurts (GRN No. 48, June 2, 2000), and the other by Procter & Gamble Co. for the use of phytosterol esters as a nutrient to enrich vegetable oil (GRN No. 53, July 24, 2000).[1]

On November 22, 2000, ADM submitted a GRAS notification to FDA, pursuant to the policy described in 62 Fed. Reg. 18938 (April 17, 1997), informing the agency of its conclusion that plant sterols and sterol esters are GRAS for use in vegetable oil spreads, dressings for salad, health bars, health drinks, and yogurt-type products to supplement the nutritive value of these products. The GRAS notification was based, in part, upon the reviews and data contained in Lipton's GRAS notification submitted as a Food Master File for plant sterol esters and the FDA's Interim Health Claim. The notification also provided other supporting data including the results of ADM's review of the safety data on plant sterols and the literature published since the Lipton information was presented to the FDA.

The GRAS notification for plant sterols and sterol esters proposes use levels for spreads and dressings for salad consistent with those proposed by Lipton, and the use levels proposed for the other three categories are set at one gram sterol equivalent per serving. These proposed levels are supported by information in the GRAS document as meeting the safety requirements for GRAS use.

While FDA's response to the ADM, Cargill and Procter & Gamble GRAS notifications have not yet been issued,[2] it is clear that significant evidence supports

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[1] Additionally, Novartis Consumer Health, Inc. submitted a GRAS notification on January 28, 2000 for the use of tall oil phytosterols as a nutrient in vegetable oil spreads to reduce the absorption of cholesterol from the gastrointestinal tract, that relied, in part, on a comparison of tall oil phytosterols to vegetable oil sterols esters and plant stanol esters (GRN No. 39). FDA responded to this notification without questions on April 24, 2000.

[2] According to the FDA proposed rule on GRAS notifications, the agency will respond within 90 days of receipt of the notice. 62 Fed. Reg. 18961 (proposed 21 C.F.R. § 170.36(e)).

the safety of the use of plant sterol esters in other conventional foods at the level necessary to justify a health claim. Thus, ADM urges FDA to conclude, as it did with plant stanol esters, that the requirements of § 101.14(b)(3)(ii) are satisfied, i.e., sufficient evidence demonstrates that the use of plant sterol esters in other food products at the level necessary to justify a health claim is "safe and lawful".

b. Analytical Method

ADM is currently developing a validated analytical method for the measurement of plant sterol esters in health bars, health drinks, and yogurt-type products. Because of the short period of time since the publication of the Interim Final Rule, it has not been possible to fully complete and validate the method for determination of sterol ester content in health drinks, health bars, and yogurt-type products. The method will be forwarded as a supplement to the FDA when the work is completed.

2. Scientific Evidence Supports the Expansion of the Interim Health Claim to Include Non-Esterified Forms of Plant Sterols

Separately, ADM requests that FDA amend interim regulation § 101.83(c)(2)(ii) to allow food containing non-esterified forms of plant sterols to include on labels and labeling the CHD health claim. As a corollary to this request, ADM urges FDA to include free plant sterols within the terms of the expanded health claim discussed in Section B.1. Additional safety and analytical information is provided in the comments below.

a. Role of Non-Esterified Forms of Plant Sterols in Reducing Serum Cholesterol

Currently the interim regulation defines the "nature of the substance" eligible to make a CHD health claim as (1) "plant sterol esters" prepared by esterifying a mixture of plant sterols containing at least 80% beta-sitosterol, campesterol, and stigmasterol (combined weight) with food-grade fatty acids and (2) "plant stanol esters" prepared by esterifying a mixture of plant stanols containing at least 80% sitostanol and campestanol (combined weight) with food-grade fatty acids. See Interim Rule § 101.83(c)(2)(ii)(A)(1) and (B)(1). Notwithstanding this description, FDA acknowledges in its preamble discussion that most of the studies

the agency reviewed concerning the cholesterol-lowering effect of plant sterol esters used vegetable oil sterols, particularly those derived from soybean oil, and most of the studies the agency reviewed concerning the cholesterol-lowering effect of plant stanol esters used vegetable oil stanols or wood-derived plant stanols. See 65 Fed. Reg. at 54705-06.

In terms of the plant sterol esters health claim, the FDA evaluated 15 studies conducted between 1953 and 2000 to elucidate the relationship of serum cholesterol and the consumption of plant sterols and plant sterol esters. In evaluating data from both free and ester forms, the petitioner (Lipton) asserted that because plant sterol esters are hydrolyzed to free sterols and fatty acids in the gastrointestinal tract and free sterols are the active moiety of plant sterol esters, "the literature on free plant sterols has a direct bearing on this petition." See 65 Fed. Reg. at 54690. The FDA agreed with this conclusion and stated that "studies of the effectiveness of free plant sterols in blood cholesterol reduction are relevant to the evaluation of the evidence in the plant sterol esters petition." Id.

Similarly, with respect to the plant stanol esters health claim, the petitioner (McNeil) submitted 21 scientific studies conducted between 1993 and 2000 in evaluating the relationship between blood cholesterol levels and plant stanol esters and plant stanols. Again, FDA agreed with the petitioner that studies of the effectiveness of free plant stanols in blood cholesterol reduction are relevant because stanol esters are hydrolyzed in the gastrointestinal tract to fatty acids and free stanols and investigators believe there is a physiological equivalence of free stanols and stanol esters in affecting blood cholesterol concentrations. 65 Fed. Reg. at 54691.

Because both the petitioners and FDA relied upon scientific studies using the non-esterified forms of the relevant nutrient, i.e., plant sterols/stanols, in support of the CHD health claim, ADM requests that FDA recognize this relationship in its Interim Final Rule by amending the "nature of the substance" provision of the interim regulation to specifically include free plant sterols. Thus, qualifying food products containing the appropriate amounts of plant sterol esters, plant stanol esters or free plant sterols could bear the interim CHD health claim.

b. Eligible Categories of Food Products

ADM also urges FDA to include free plant sterols within the terms of the expanded categories of food products proposed in Section B.1., i.e., health bars, health drinks, and yogurt-type products. As noted above, non-esterified plant sterols are substantially equivalent to the esterified compounds. Thus, the data and information submitted by Lipton and McNeil, and the additional information provided in these comments as to plant sterol esters, are fully applicable to free plant sterols. ADM further offers the following additional comments.

(i) Safety of Free Plant Sterols

The GRAS notification submitted by ADM on November 22, 2000, to FDA, also informed the agency of its conclusion that free plant sterols are GRAS for use in vegetable oil spreads, dressings for salad, health bars, health drinks, and yogurt-type products to supplement the nutritive value of these products. The use levels proposed are about one gram free sterol for health drinks, health bars, and yogurt-type products. Use levels for spreads and dressings for salad are consistent with the free sterol equivalent level proposed in the Lipton petitions. The GRAS notification for free sterols was based, in part, upon the reviews and data contained in Lipton's GRAS notification submitted as a Food Master File for plant sterol esters and the FDA's Interim Health Claim. The notification also provided other supporting data including the results of ADM's review of the safety data on plant sterols and the literature published since the Lipton information was presented to the FDA.

As noted above, Lipton informed FDA of its determination that plant sterol esters were GRAS on January 11, 1999. This notification was based on data from studies including sterol esters and free sterols and the determination that sterol esters are converted in the gastrointestinal tract to free sterols.[3] Consistent with

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[3] The GRAS panel convened by Novartis to review the GRAS status of tall oil phytosterols also concluded that the ester forms that are present in vegetable oil sterol esters and plant stanol esters are rapidly de-esterified in vivo. See FDA Response letter to Novartis dated April 24, 2000.

FDA's reliance on free sterol literature with regard to the ester, it is ADM's position that the safety literature on sterol esters may be used to support the GRAS determination for free-sterols.

While FDA has not yet responded to this notification, ADM is confident, based on the recently published literature on sterol esters and free sterols, the agency's response to Lipton's GRAS conclusion, and the other GRAS notifications subsequently filed by Cargill and Procter & Gamble, that there is significant evidence to support the safety of the use of free plant sterols in spreads, dressings for salads, health bars, health drinks, yogurt-type products, and other foods at the levels necessary to justify a health claim.

(ii) Analytical Method

The analytical method discussed in Section B. 1. b. for plant sterol esters is being validated to measure both plant sterol esters and free sterols. Because this analytical method will permit an accurate determination of the amount of free sterols in health bars, health drinks and yogurt-type products, the comments offered in Section B. 1. b. apply equally to this Section and are incorporated by reference.

C. CONCLUSION

For the reasons set forth above, ADM urges FDA to amend the Interim Final Rule for plant sterol/stanol esters and CHD to (1) expand the categories of food products eligible to make the CHD health claim to include health bars, health drinks, and yogurt-type products and (2) include the non-esterified forms of plant sterols within the definition of the "nature of the substance" eligible to make the CHD health claim.

Very truly yours,

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